REMARKS

Claims 1-56 are pending of which claims 1-28 and 45-54 are withdrawn from examination as directed to non-elected inventions. Claims 29, 30, 33-38, and 41-44 are amended herein and claims 55 and 56 are added. Support for the claim amendments is outlined below. Applicants respectfully request reconsideration of this application in view of the amendment and remarks set forth in this Reply.

Amendments to the Claims:

Claims 29, 30, 33-38, and 41-44 are amended herein. Applicants believe that no new matter is being added as support for these claims amendment can be found in the specification as follows:

- Claim 29: This claim is amended to more clearly define the modified biopolymer in the form of a structural formula. Support can be found at least at page 9, line 12 to page 10, line 12; and page 14, lines 6-18.

- Claims 30 and 38: This claim is amended to correct a typographical error.

- Claims 33, 34, 41 and 42: These claims are amended to recite terms having antecedent basis in amended claims 29 and 37 and set forth preferred embodiments of the invention. Support for these claims amendment can be found in the specification at least at page 5, lines 31-33, page pages 9-11, and in the Examples.

- Claims 35 and 43: These claims are amended to the R group having antecedent basis in respective claims 29 and 37.

- Claims 36 and 44: These claims are amended to the linker L having antecedent basis in respective claims 29 and 37.

- Claim 37: This claim is amended to more clearly define the modified biopolymer in the form of a second structural formula. Support can be found at least at pages 11-12; and page 14, lines 6-18.

- Claims 55: This claim is added to further define a degree of modification of the modified biopolymer in the case of a preferred embodiment, HA-NEA. Support for this amendment can be found in the specification at least in the Examples 2, 3 and 4. And,

- Claim 56. This claim is added to further define a degree of modification of the modified biopolymer in the case of a preferred embodiment, HA-NEA. Support for this amendment can be found in the specification at least in the Examples 9 and 10.

Rejection of Claims under §112, First Paragraph:

Claims 33, 34-36, 41, and 42-44 are rejected for reciting a term having no antecedent basis in the respective independent claims 29 and 37. Applicants have amended the claims to recite terms having antecedent basis as outlined above. Applicants believe these amendments complies with the Examiner's requests and thus respectfully request that this rejection be withdrawn.

Rejection of Claims under §103(a):

Claims 29-36 are rejected as being unpatentable over a combination of references—Pouyani et al. in view of Latham et al, Zara et al., Prestwich et al. and Bernkop-Schnurch et al. Applicants have amended independent claim 29 to more specifically recite the subject matter they believe to be their invention. Applicants submit that claims 29-36 as amended and claim 55 are patentable over the cited art.

In particular, claim 29 now defines a modified biopolymer according to a structural formula (G-CO-R-L-SS-M) in which the biopolymer is bound to a disulfide moiety, -SS-M, by a carbonyl group as an alkylamide (-C(O)R-L-, where R is an amino group and L a lower alkyl group), or an alkylester linkage (-C(O)R-L-, where R is an oxygen atom and L a lower alkyl group). Applicants respectfully submit that none of the cited references, taken alone or combined, teaches or suggests the presently claimed invention.

Pouyani does not teach or suggest biopolymers as in claims 29-36 and 55. Pouyani only teaches derivatives of hyaluronic acid (HA) in which a linking group is bound to the HA by a hydrazido functional group (HA-C(O)-NH-NH-X). Pouyani does not teach or suggest HA derivative having the alkylamide or alkylester as claimed in the present claims 29-36 and 55. Also, Pouyani teaches the presence of multifunctional groups, such as dihydrazido groups -C(O)-NH-NH-C(O)-, within the linking arm between the dihydrazide bound to the HA and the disulfide group. The linking arms of Pouyani thus can be distinguished from the lower alkyl arm, L, in the present claims 29-36 and 55.

Further, Pouyani teaches away from preparing amide or ester derivatives of HA. At page 339, col. 2, last paragraph, Pouyani states that reaction of HA with an amine in the presence of EDC did not lead to the formation of the desired amide because "the putative *O*-acylurea intermediate rearranged in preference to trapping by the diamine nucleophile." Pouyani further explains that "to take advantage of the further functionalization of HA, a different strategy was required," such as with the use of dihydrazides because of their low pKa values, they maintain their nucleophilicity at pH = 4.75 in comparison with aliphatic amines which become protonated at that pH. Thus Pouyani does not provide the necessary incentive to modify its teachings or combine its teachings with other references to arrive at the presently claimed invention and should therefore be withdrawn from this rejection.

Prestwich does not cure the deficiencies of the primary reference, Pouyani. Like Pouyani, Prestwich only teaches HA modified through hydrazide linkages (HA-C(O)-NH-NH-X) and linkers with multi hydrazide groups between the HA and the disulfide moiety. Like Pouyani, Prestwich also fails to suggest any modification of the linkers that could lead a person skilled in the art at the presently claimed invention. Thus, either taken alone or in combination with Pouyani, Prestwich fails to teach or suggest the presently claimed invention.

Zara also does not cure the deficiencies of the primary reference Pouyani. Zara teaches crosslinkers that all comprise at least the core functionality of an α-amino acid (i.e. X-C(O)-CH(NH_2)-Y-Z) between a terminal amino group (within X) and a disulfide group (within Z), which can be distinguished from the lower alkyl arm, L, in the present claims 29-36

and 55. Zara does not suggest any modification of this core to arrive at compound of the claimed invention.

Latham does not cure the deficiencies of the primary reference, Pouyani. Latham teaches oligonucleotide-transport agent conjugates with disulfide linkers. Latham does not even teach or suggest a biopolymer having carboxylic acid groups as a transport agent. Latham teaches specifically as transport agent three biocompatible polymers, all of which do NOT have carboxylic groups: cellulose, polyethylene glycol and polyvinyl alcohol. Further, Latham does not teach how the cellulose, used as a transport agent, is bound to the disulfide linker. Latham does not teach or suggest further modifying the biocompatible polymer to arrive at a biopolymer having carboxylic groups, even less how reacting carboxylic group to form amide or ester bound to attach a disulfide linker as in the presently claimed invention. Thus, even when combined with the primary reference, Latham does not teach or suggest the presently claimed invention.

In summary, all the cited references fail to teach the claimed invention as a whole. Further, none of the references provides the necessary incentive to modify any of their teachings to arrive at the claimed invention. A combination of references must not be arbitrary; an incentive to modify the teaching of a prior art reference in accordance with the teaching of another must be found in the references themselves and not be derived from the applicants' invention using the Applicants' claims as a blueprint. *Interconnect Planning Corp. v. Feil*, 774 F.2d. 1132, 227 USPQ 543 (Fed. Cir 1985); *In Re Gorman,* 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991). Accordingly, Applicants respectfully submit that the present amended claims 29-36 and 55 are patentable over the cited combination of references.

Claims 37-44 are rejected as unpatentable over a combination of references —Pouyani et al. in view of Latham et al, Zara et al., Prestwich et al. and Margel et al. Applicants have amended independent claim 37 to more specifically recite the subject matter they believe to be their invention. Applicants submit that claims 37-44 as amended and new claim 56 are patentable over the cited art.

In particular, claim 37 now defines a modified biopolymer according to a structural formula (G-C-R-L-SS-M) in which the biopolymer is bound to a disulfide moiety, -SS-M, by a

methylaminoalkyl linking group (-C-R-L-, where R is an amino group and L a lower alkyl group). Applicants respectfully submit that none of the cited references, taken alone or combined, teaches or suggests the presently claimed invention.

Pouyani does not teach or suggest biopolymers as in claims 37-44 and 56. The observations about Pouyani for the previous set of claims (29-36 & 55) are equally applicable to this set of claims (37-44 & 56). Pouyani only teaches derivatives of hyaluronic acid (HA) in which a linking group is bound to the carboxylic groups of the HA with a hydrazide functional group (HA-C(O)-NH-NH-X). Pouyani does not teach or suggest HA derivative having a methylaminoalkyl as claimed in the present claims 37-44 and 56. Also, Pouyani teaches the presence of multifunctional groups, such as dihydrazides groups -C(O)-NH-NH-C(O)-, within the linking arm between the dihydrazide bound to the HA and the disulfide group. The linkers of Pouyani thus can be distinguished from the lower alkyl arm, L, in the present claims 37-44 and 56.

Prestwich does not cure the deficiencies of the primary reference, Pouyani. The observations about Prestwich for the previous set of claims (29-36 & 55) are equally applicable to this set of claims (37-44 & 56). Like Pouyani, Prestwich only teaches HA modified through its carboxylic groups to hydrazide linkages (HA-C(O)-NH-NH-X) and linkers with multi hydrazide groups between the HA and the disulfide moiety. Like Pouyani, Prestwich also fails to suggest any modification of the linkers that could lead a person skilled in the art at the presently claimed invention. Thus, either taken alone or in combination with Pouyani, Prestwich fails to teach or suggest the presently claimed invention.

Zara also does not cure the deficiencies of the primary reference Pouyani. The observations about Zara for the previous set of claims (29-36 & 55) are equally applicable to this set of claims (37-44 & 56). Zara only teaches crosslinkers always comprising at least the core functionality of an α-amino acid (i.e. X-C(O)-CH(NH_2)-Y-Z) between a terminal amino group (within X) and a disulfide group (within Z). Zara does not suggest any modification of this core to arrive at compound of the claimed invention.

Latham does not cure the deficiencies of the primary reference, Pouyani. The observations about Latham for the previous set of claims (29-36 & 55) are equally applicable to

this set of claims (37-44 & 56). Latham teaches oligonucleotide-transport agent conjugates with disulfide linkers. Latham does not even teach or suggest a biopolymer having carboxylic acid groups as a transport agent. Latham teaches specifically as transport agent three biocompatible polymers which do not have carboxylic groups: cellulose, polyethylene glycol and polyvinyl alcohol. Further, Latham does not teach how the cellulose, used as a transport agent, is bound to the disulfide linker. Latham does not teach or suggest further modifying the biocompatible polymer to arrive at a biopolymer having carboxylic groups, even less how reacting carboxylic group to form amide or ester bound to attach a disulfide linker as in the presently claimed invention. Thus, even when combined with the primary reference, Latham does not teach or suggest the presently claimed invention.

Margel does not cure the deficiencies of the primary reference. Margel teaches methods of derivatizing polysaccharide materials to immobilize proteins thereon. However, Margel does not teach or suggest modified polysaccharide having the aminolakyl disulfide moiety (-R-L-SSM) as presently claimed. Thus, even when combined with the primary reference, Margel does not teach or suggest the presently claimed invention.

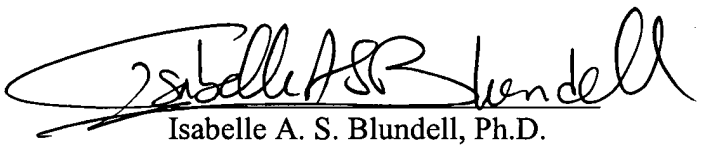
In summary, all the cited references fail to teach the claimed invention as a whole. Further, none of the references provides the necessary incentive to modify any of their teachings to arrive at the claimed invention. A combination of references must not be arbitrary; an incentive to modify the teaching of a prior art reference in accordance with the teaching of another must be found in the references themselves and not be derived from the applicants' invention using the Applicants' claims as a blueprint. *Interconnect Planning Corp. v. Feil*, 774 F.2d. 1132, 227 USPQ 543 (Fed. Cir 1985); *In Re Gorman,* 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991). Accordingly, Applicants respectfully submit that the present amended claims 37-44 and 56 are patentable over the cited combination of references.

Applicants believe that all issues raised in the Office Action have been addressed in this reply and kindly request favorable reconsideration of the instant application.

FEE PAYMENT

Applicants hereby authorize to charge Deposit Account 07-1074 for payment of fees due, such as the three-month extension of time or any additional fee.

Respectfully submitted,



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